

## 7. REGULATIONS AND ADVISORIES

The World Health Organization classified nickel compounds as Group 1 carcinogens (human carcinogens) and metallic nickel as a Group 2B carcinogen (possible human carcinogen) (IARC 1990). In an attempt to reduce the prevalence of nickel sensitivity, the European Union has passed a directive to restrict the use of nickel beginning in February 1996 (Delescluse and Dinét 1994). The directive forbids the use of nickel in objects introduced into pierced ears and other parts of the human body during epithelialization of the wound. It forbids the use of nickel in products placed in direct and prolonged contact with the skin (e.g., earrings, watches, clothing accessories). The use of nickel is also forbidden in accessories that are plated with another metal, except if the plating is strong enough to restrict liberation of nickel to less than  $0.5 \mu\text{g}/\text{cm}^2/\text{week}$  during a normal use of 2 years.

In this profile, a chronic-duration inhalation MRL of  $2 \times 10^{-4}$  mg nickel/ $\text{m}^3$  has been derived based on a NOAEL of 0.03 mg nickel/ $\text{m}^3$  as nickel sulfate that was identified in a 2-year study of nickel sulfate in rats (NTP 1996c). Chronic active inflammation of the lungs was observed at  $\geq 0.06$  mg nickel/ $\text{m}^3$ . The inflammation was described as follows: multifocal, minimal-to-mild accumulations of macrophages, and neutrophils and cell debris within alveolar spaces. The prevalence of lung fibrosis was also significantly increased at  $\geq 0.06$  mg nickel/ $\text{m}^3$ . This chronic-duration inhalation MRL should also be protective of intermediate-duration exposure.

National and state guidelines and regulations regarding exposure to nickel and its compounds are summarized in Table 7-1. The EPA considers nickel refinery dust and nickel subsulfide as class A carcinogens, and therefore an inhalation unit risk has been determined. The unit risk of  $4.8 \times 10^{-4}$  per ( $\mu\text{g}/\text{m}^3$ ) (IRIS 1996) is based on human epidemiology data showing an increased risk of lung and nasal cancers in refinery workers exposed to nickel refinery dust that was principally nickel subsulfide (Chovil et al. 1981; Enterline and Marsh 1982; Magnus et al. 1982). Concentrations of  $2 \times 10^{-4}$ ,  $2 \times 10^{-5}$ , and  $2 \times 10^{-6}$  mg/ $\text{m}^3$  are associated with risk levels of 1 in 10,000, 1 in 100,000, and 1 in 1,000,000, respectively (IRIS 1996). DHHS considers nickel and nickel compounds as reasonably anticipated to be carcinogens (DHHS 1994).

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**TABLE 7-1. Regulations and Guidelines Applicable to Nickel**

Agency	Description	Information	References
<u>INTERNATIONAL</u>			
IARC	Carcinogenic classification Nickel compounds Metallic nickel	Group 1 <sup>a</sup> Group 2B <sup>b</sup>	IARC 1994
<u>NATIONAL</u>			
Regulations:			
a. Air:			
OSHA	TWA (nickel metal, and insoluble compounds) TWA (nickel, soluble compounds)	1 mg/m <sup>3</sup> 1 mg/m <sup>3</sup>	OSHA 1993 (58 FR 35338)
b. Other:			
EPA	RQ  Nickel Nickel chloride Nickel hydroxide Nickel nitrate Nickel sulfate	  100 pounds 100 pounds 10 pounds 100 pounds 100 pounds	EPA 1996b (60 FR 35991)
Guidelines:			
a. Air:			
ACGIH	Nickel Metal Insoluble compounds Soluble compounds Nickel sulfide Intended changes Nickel Elemental/metal Soluble compounds Insoluble compounds Nickel subsulfide (includes nickel sulfide roasting and dust)	  1.0 mg/m <sup>3</sup> 1.0 mg/m <sup>3</sup> 0.1 mg/m <sup>3</sup> 1.0 mg/m <sup>3</sup> , A1 <sup>e</sup>   0.5 mg/m <sup>3</sup> 0.05 mg/m <sup>3</sup> , A4 <sup>f</sup> 0.1 mg/m <sup>3</sup> , A1 <sup>e</sup> 0.05 mg/m <sup>3</sup> A1 <sup>e</sup>	ACGIH 1996     ACGIH 1996 ACGIH 1996
NIOSH	REL TWA (metal, soluble, insoluble, and inorganic)	0.015 mg/m <sup>3</sup>	NIOSH 1994c
EPA	Inhalation q <sub>1</sub> * (nickel refinery dust)	2.4×10 <sup>-4</sup> (µg/m <sup>3</sup> ) <sup>-1</sup>	IRIS 1996

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**TABLE 7-1 (continued)**

Agency	Description	Information	References
<u>NATIONAL (Cont.)</u>			
b. Water:			
EPA	Health advisories:		EPA 1996a
	1-day (child)	1.0 mg/L	
	10-day (child)	1.0 mg/L	
	Longer term (child)	0.5 mg/L	
	Longer term (adult)	1.7 mg/L	
	Lifetime (adult)	0.1 mg/L	
	DWEL (Drinking Water Equivalent Level)	0.6 mg/L	
EPA	Ambient water quality criteria for protection of human health		EPA 1995b (60 FR 44120)
	Ingesting water and organisms	610 µg/L	
	Ingesting organisms only	4.6 mg/L	
c. Other:			
EPA	RfD (oral) - Nickel	0.02 mg/kg/day	IRIS 1996
EPA	Carcinogen classification	Group A <sup>d</sup>	IRIS 1996
	Nickel refinery dust and nickel subsulfide		
NTP	Cancer classification	reasonably anticipated to be carcinogens	DHHS 1994
	Nickel and certain nickel compounds (nickel acetate, nickel carbonate, nickel carbonyl, nickel hydroxide, nickelocene, nickel oxide, nickel subsulfide)		
FDA	Bottled water contaminant level (proposed)	0.1 mg/L	FDA 1993 (58 FR 41612)
<u>STATE</u>			
Regulations and Guidelines:			
a. Air:	Acceptable ambient air concentrations		NATICH 1996
	Nickel		
Arizona		5.7 µg/m <sup>3</sup> (1 hour)	
		1.5 µg/m <sup>3</sup> (24 hour)	
		0.004 µg/m <sup>3</sup> (1 year)	
Connecticut		5.0 µg/m <sup>3</sup> (8 hour)	

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**TABLE 7-1 (continued)**

Agency	Description	Information	References
<u>STATE</u> (Cont.)			
Florida (Ft Lauderdale)		0.01 mg/m <sup>3</sup> (8 hour)	
Florida (Pinella)		0.5 µg/m <sup>3</sup> (8 hour)	
		0.12 µg/m <sup>3</sup> (24 hour)	
		0.0042 µg/m <sup>3</sup> (1 year)	
Kansas		0.00417 µg/m <sup>3</sup> (1 year)	
Louisiana		0.21 µg/m <sup>3</sup> (1 year)	
Massachusetts		0.27 mg/m <sup>3</sup> (24 hour)	
		0.18 µg/m <sup>3</sup> (1 year)	
		0.0042 µg/m <sup>3</sup> (1 year)	
Minnesota			
Montana		0.79 µg/m <sup>3</sup> (24 hour)	
		0.13 µg/m <sup>3</sup> (1 year)	
Nevada		0.002 mg/m <sup>3</sup> (8 hour)	
New York		3.3 µg/m <sup>3</sup> (1 year)	
North Carolina		0.006 µg/m <sup>3</sup> (24 hour)	
North Dakota		0.01 mg/m <sup>3</sup> (8 hour)	
Oklahoma		0.15 µg/m <sup>3</sup> (24 hour)	
Pennsylvania		0.24 µg/m <sup>3</sup> (1 year)	
Rhode Island		0.002 µg/m <sup>3</sup> (1 year)	
South Carolina		0.5 µg/m <sup>3</sup> (24 hour)	
Texas		0.15 µg/m <sup>3</sup> (30 minute)	
		0.015 µg/m <sup>3</sup> (1 year)	
Vermont		0.0033 µg/m <sup>3</sup> (1 year)	
Virginia		1.7 µg/m <sup>3</sup> (24 hour)	

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TABLE 7-1 (continued)

Agency	Description	Information	References
<u>STATE</u> (Cont.)			
Washington		3.3 $\mu\text{g}/\text{m}^3$ (24 hour)	
Connecticut	Nickel oxide	0.3 $\mu\text{g}/\text{m}^3$ (8 hour)	
South Carolina	Nickel sulfate	5 $\mu\text{g}/\text{m}^3$ (24 hour)	
Connecticut	Nickel subsulfide	5.0 $\mu\text{g}/\text{m}^3$ (8 hour)	
Kansas		0.00208 $\mu\text{g}/\text{m}^3$ (1 year)	
Nevada		24 $\mu\text{g}/\text{m}^3$ (8 hour)	
New York		0.1 $\mu\text{g}/\text{m}^3$ (1 year)	
North Carolina		0.0021 $\mu\text{g}/\text{m}^3$ (1 year)	
Texas		1 $\mu\text{g}/\text{m}^3$ (1 year) 10 $\mu\text{g}/\text{m}^3$ (30 minute)	
b. Water:	Drinking water quality standards and guidelines		FSTRAC 1990
Arizona		150 $\mu\text{g}/\text{L}$	
Kansas		150 $\mu\text{g}/\text{L}$	
Maine		150 $\mu\text{g}/\text{L}$	
Minnesota		150 $\mu\text{g}/\text{L}$	
New Hampshire		150 $\mu\text{g}/\text{L}$	
Rhode Island		150 $\mu\text{g}/\text{L}$	
Vermont		150 $\mu\text{g}/\text{L}$	
	Drinking water supply standards		
Arizona		140 $\mu\text{g}/\text{L}$	CELDS 1994
Indiana		13.4 $\mu\text{g}/\text{L}$	
Kentucky		13.4 $\mu\text{g}/\text{L}$	
Mississippi		607 $\mu\text{g}/\text{L}$	
West Virginia		510 $\mu\text{g}/\text{L}$	
Wisconsin		0.17 $\mu\text{g}/\text{L}$	

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**TABLE 7-1 (continued)**

Agency	Description	Information	References
<u>STATE</u> (Cont.)			
North Carolina	Groundwater standards	0.15 µg/L	CELDS 1994

<sup>a</sup>Group 1: Human carcinogen<sup>b</sup>Group 2B: Possible human carcinogen<sup>c</sup>This value is the lowest reliable detectable concentration of nickel measurable by the methods recommended by NIOSH (1977).<sup>d</sup>Group A: Human carcinogen<sup>e</sup>Group A1: Confirmed human carcinogen<sup>f</sup>Group A4: Not classifiable as a human carcinogen

AADI = acceptable adult daily intake; ACGIH = American Conference of Governmental Industrial Hygienists; CFR = Code of Federal Regulations; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IARC = International Agency for Research on Cancer; IRIS = Integrated Risk Information System; Ni = nickel; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration; REL = Recommended Exposure Limit; RfD = Reference Dose; RQ = reportable quantity; STEL = Short Term Exposure Limit; TLV = Threshold Limit Value; TPQ = Threshold Planning Quantity; TWA = Time-Weighted Average; WHO = World Health Organization

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The oral reference dose (RfD) for nickel is 0.02 mg/kg/day (IRIS 1996). The RfD is based on the 5-mg-nickel/kg/day NOAEL identified in the Ambrose et al. (1976) 2-year study in rats. The effect level in this study was 50 mg/kg/day, a dose associated with changes in body and organ weights. The RfD was calculated using an uncertainty factor of 300 (10 for interspecies extrapolation, 10 to protect sensitive individuals, and 3 to account for inadequacies in reproductive studies) (Ambrose et al. 1976; RTI 1988a, 1988b). EPA (IRIS 1996) states that the RfD is at a level that will not sensitize individuals to nickel, but that it may not protect individuals who are already sensitized to nickel.

The EPA maximum contaminant level (MCL) for nickel of 0.1 mg/L has been remanded (EPA 1995a). This action was the result of a lawsuit filed by the Nickel Development Institute and other industry parties regarding the methodology for determining the MCL. EPA agreed to remand the MCL because it did not fully address in the public record industries' comments pertaining to the methodology for deriving the MCL for nickel.

Nickel and its compounds are regulated by the Clean Water Effluent Guidelines for the following industrial point sources: the manufacturing of iron, steel, nonferrous metals, and batteries; timber products processing; electroplating; metal finishing; ore and mineral mining; paving and roofing; paint and ink formulating; porcelain enameling; copper forming; nonferrous metal forming; and industries that use, process, or manufacture organic and inorganic chemicals, gum and wood, and carbon black (EPA 1988).

